NCI-FREDERICK ANIMAL CARE AND USE NEWSLETTER

February 2004

NEWSLETTER CONTENTS

Animal Care & Use Committee Functions

The goal of the NCI-Frederick Animal Care and Use Committee (ACUC) is to ensure the humane care and use of animals used in biomedical research projects at the NCI-Frederick. This committee is comprised of individuals representing NCI-Frederick scientists, veterinarians, occupational safety, and the general public. It is the responsibility of the ACUC to ensure adherence to the Public Health Service Policy, the Animal Welfare Act, the US Government Principles, and the Guide for the Care and Use of Laboratory Animals, which govern the use of animals in biomedical research. The ACUC is constantly challenged with balancing its requirement to ensure the well-being of our animals while trying to efficiently and effectively meet the needs of its investigative research staff. One way in which the ACUC addresses this issue is working hand-in-hand with investigators to assist with proposal preparation, submission, review, and implementation. It is this teamwork approach that ensures compliance and results in quality animal care. Remember … quality animal care is a fundamental step in ensuring reliable scientific data. Each animal user plays an important role in implementing these high standards of quality care at the NCI-Frederick.

Post-Approval Monitoring

There are times when the ACUC is unfamiliar with a procedure that is requested by an investigator or the expected outcome of an experiment. In an effort to fulfill a researcher's request and to ensure the humane care of the animals, the ACUC will permit an investigator to proceed with the proposed procedure with a stipulation that the Laboratory Animal Medicine staff observe the procedure and report back to the ACUC with their findings (also known as post-approval monitoring). Post-approval monitoring has become a standard practice in the field of laboratory animal science. The post-approval monitoring process, where stipulated, is a requirement. It is very important that the investigator and/or technical staff contact the ACUC Coordinator as instructed in their approval notice. Please be sure that the ACUC Coordinator and Attending Veterinarian have the appropriate time(s) and place(s) for scheduled procedures.

Monoclonal Antibody Production

The ACUC has recently revised its *Guidelines for Ascites Production*[1] because monoclonal antibody production has become an important animal welfare issue. The ascites method, which until quite recently was the standard technique worldwide, may cause considerable pain and distress in the animals used to produce the monoclonal antibodies.[2] It is this fact that has prompted the laboratory animal science community to focus on the available *in vitro* alternatives that now exist. The ACUC currently requires scientific justification for *in vivo* ascites production of monoclonal antibodies. In addition, the ACUC requests that an investigator indicate (1) if he/she has considered *in vitro* techniques and (2) the rationale for not utilizing the non-animal model. In an effort to evaluate the efficacy of various *in vitro* antibody production techniques, the Laboratory Animal Science Program has decided to select several antibodies to compare the *in vitro* vs. *in vivo* production methods. These findings will be brought to the ACUC for review and deliberation at a future meeting.

Neonatal Euthanasia

In an ongoing effort to refine research methodologies, the ACUC and LAM reviewed the neonatal euthanasia methods recommended in the *Guidelines for Euthanasia of Rodents Using Carbon Dioxide*.[1] As a result, LAM was requested to conduct a pilot study to (1) evaluate the various euthanasia techniques and (2) select the most effective and humane methods. LAM is in the process of conducting their study and findings will be reported to the ACUC within the next few months. The current guidelines will be modified as necessary based on these findings.

Tumor Regression Studies

As a friendly reminder … the ACUC would like to emphasize that careful attention should be paid to any animal exhibiting an ulcerated and/or necrotic tumor with a break in the overlying skin. To deter cannibalization, any animal exhibiting this type of tumor should be separated immediately and singly housed until tumor regression is complete. Personnel are responsible for ensuring adherence to ACUC approved regression timelines and endpoints as described in the animal study proposal.

Revised Guidelines and Policies

The ACUC has recently revised the following Guidelines and Policies[1]*:*

Guidelines for Ascites Production – Revised February 2004
Responsibilities of Investigators Maintaining Mutant Strains of Mice – Revised November 2003
Guidelines Involving Experimental Neoplasia Protocols – Revised November 2003

Building 567 – Parvovirus Update

For many years, minute virus of mice (MVM) was recognized as the sole parvovirus of laboratory mice. Recent research has confirmed natural infection with a newly recognized serogroup. The prototype isolate was initially called mouse orphan parvovirus, but has been recently renamed mouse parvovirus (MPV). Here is some useful information regarding these two parvoviruses:

Minute Virus of Mice (MVM)

Clinical Signs: MVM, in contrast to MPV, is not thought to cause persistent infection. Infection in immunocompetent adult mice usually lasts less than 3 weeks. **Pathology:** Natural infection or experimental inoculation ofadult mice appears to be nonpathogenic. **Diagnosis:** ELISA serology is the primary method of detection with a high degree of confidence. Furthermore, MVM can be differentiated from MPV using-virus specific VP-2 antigens.

Mouse Parvovirus (MPV)

MPV, on the other hand, causes persistent infection in infant and adult mice, a property that differentiates it from MVM. **Clinical Signs:** A MPV infection is clinically silent in infant mice and in adult immunocompetent or immunodeficient mice. **Pathology:** Acute infection, though mild, is widespread involving lung, liver, kidney and lymph organs. Lymphocytotropism is characteristic of acute and persistent MPV infection. **Diagnosis:** Serological detection is not uniform across age groups and may become even more nebulous when one considers background stock and strain differences. Younger animals are thought to provide more uniform serological results. MPV-specific ELISA is available. PCR is sensitive and specific but only effective in actively infected animals and therefore requires access to tissues usually obtained at necropsy. **Research Complications:** Murine parvoviruses can distort biological responses that depend on cell proliferation. For MPV, such effects are seen on immune function and include augmentation or suppression of humoral and cellular immune responses.

New Animal Study Proposal Form

Please use the current version of the Animal Study Proposal Form[1] to expedite review of your study …
http://web.ncifcrf.gov/rtp/lasp/acuc/proposal.asp

For additional information or assistance …
please visit the ACUC website at

http://web.ncifcrf.gov/rtp/lasp/acuc/main.asp

Some Helpful Web Links

Alternatives to Animal Testing on the Web
http://altweb.jhsph.edu/
Office of Laboratory Animal Welfare
http://grants.nih.gov/grants/olaw/olaw.htm
IACUC.org
http://www.iacuc.org/
Research Training
https://216.205.76.49/researchtraining/

[1] Links to this information can be found on the NCI-Frederick ACUC website
[2] Adapted from Johns Hopkins *ALTWEB* website
[3] Laboratory Animal Medicine, 2nd edition, 2002